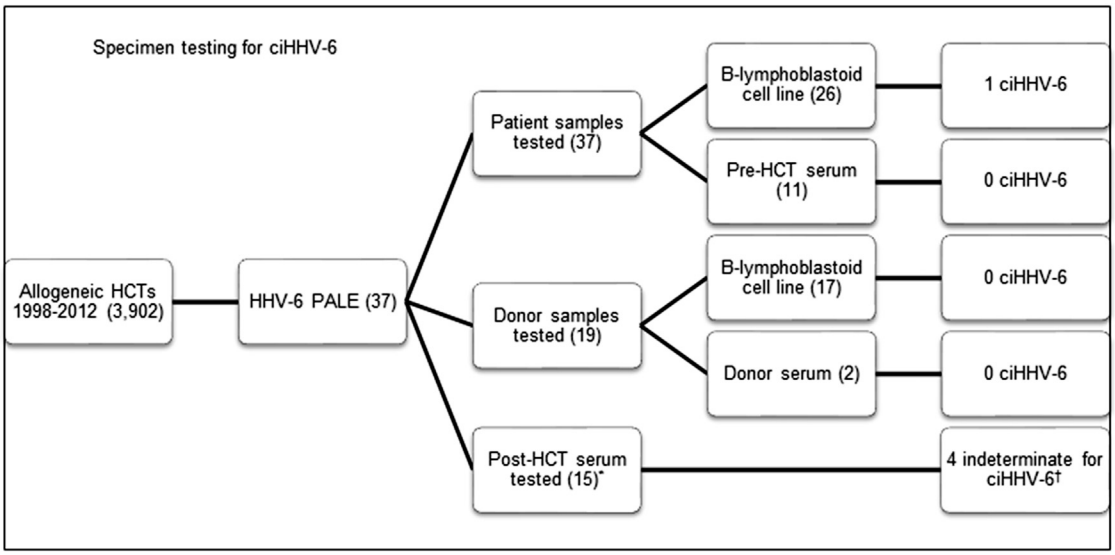

Figure. Specimen testing for ciHHV-6

Results: Among 3,902 patients undergoing allogeneic HCT at our institution from 1998-2012, 37 (0.95%) met criteria for HHV-6-PALE. This cohort had 16 double cord blood, 13 peripheral blood (PBSCT), and 8 bone marrow HCTs. Median maximum CSF HHV-6 viral load (VL) was 10,000 copies/ml (range, 54-450,000). Twenty-six cellular and 11 serum pre-HCT patient samples were tested for ciHHV-6 (**Figure**). CiHHV-6 was detected in 1 of 37 samples (2.7%; 95% CI, 0.07-14.5%). This patient developed HHV-6-PALE D+12 after PBSCT with maximum CSF VL of 250,000 copies/ml and died on D+40 from complications of autopsy-confirmed encephalitis. Nineteen donor samples (17 cellular, 2 serum) tested negative for ciHHV-6. Late post-engraftment serum samples were tested in cases without available donor samples; 4 of 15 had HHV-6 DNA detected but were indeterminate for ciHHV-6 (**Figure**).

Conclusions: This is the first epidemiologic study of the prevalence of ciHHV-6 in patients with HHV-6 PALE and included the largest reported cohort of HHV-6-PALE cases to date. CiHHV-6 was identified in one patient, which has never been described in this setting. Sequencing of pre and post-HCT viruses, as well as histopathologic testing of brain tissue, is in process. Although there is no clear evidence of ciHHV-6 enrichment in this cohort, the detection and poor outcome in the described case underscores the need for a large, multi-center study to determine the impact of ciHHV-6 on outcomes.

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Comparison of Fludarabine and Total Body Irradiation (FluTBI) to Fludarabine without TBI (Flu) Based Nonmyeloablative Conditioning (NMA) Prior to Hematopoietic Cell Transplantation (HCT) for Lymphoma

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NMA doses of FluTBI result in successful donor chimerism and have the objective of controlling disease through a graft-versus-tumor effect. Other regimens without irradiation were developed, mainly for treatment of lymphoma, yet comparisons of HCT outcomes remain scant. We compared 382 FluTBI recipients to 515 Flu recipients prior to HCT from 2001 to 2011 and reported to the Center for International Blood and Marrow Transplant Research (CIBMTR). Patients were 40 years or older with lymphoma and received matched sibling, HLA matched at 8/8 or 7/8 unrelated donor (URD) bone marrow (BM) or peripheral blood (PBSC) grafts. FluTBI cohort had a higher number of patients with Karnofsky performance score (KPS) <90% (32% vs. 22%), more chronic lymphocytic leukemia (41% vs. 33%), more URD (68% vs. 51%), more PBSC (94% vs. 85%), less anti-thymocyte globulin use (11% vs. 15%), less rituximab in the conditioning (7% vs. 40%), and more mycophenolate mofetil-based graft vs. host disease prophylaxis (GVHD, 87% vs. 15%) compared to Flu. Impact on hematopoiesis differed according to the regimen with 24% and 43% of patients never dropping the absolute neutrophil count <500/μL and platelets <50,000/μL, respectively, with FluTBI comparing to 2% and 24% with Flu. Cumulative incidences at 100 days of grades II-IV and III-IV acute GVHD were 22% and 15% with FluTBI; and 17% (p=0.04) and 10% (p=0.02) for Flu, respectively. Corresponding rates of chronic GVHD at 1 year were 54% and 44% (p=0.004). Cumulative incidences at 3 years of transplant related mortality were 28% and 23% (p=0.13), and of progression were 36% and 34% (p=0.63) for FluTBI and Flu respectively. Multivariate analysis of TRM, progression, treatment failure and mortality showed no difference in outcomes according to the conditioning regimen. Variables associated with higher mortality were age 50-59y (Hazard Ratio [HR] 1.31, p=0.03) and ≥60y (HR 1.66, p<0.001) compared to 40-49y; KPS <90% (HR 1.49, p<0.001); and recipients of 8/8 matched URD (HR 1.28, p=0.02) and 7/8 matched URD (HR 1.94, p<0.001) compared to sibling donor HCT. The three-year probabilities of progression free survival were 40% and 41% (p=0.81), and overall survival were 50% and 55% (p=0.14) after adjusting for factors from the

multivariate analysis. TBI regimens have less impact on blood counts immediate post-transplant period. Despite higher rates in acute and chronic GVHD with FluTBI, overall outcomes after HCT are comparable to non-TBI containing NMA regimens for lymphoma.

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Pretransplant Immunosuppression Followed By Reduced Toxicity Conditioning and Stem Cell Transplantation in High Risk Thalassemia

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Patients with class 3 thalassemia with high-risk features for adverse events after high-dose chemotherapy with hematopoietic stem cell transplantation (HSCT) are difficult to treat, tending to either suffer serious toxicity or fail to establish stable graft function. We performed HSCT in 21 such patients age $\geq$7 years and hepatomegaly using a novel approach with pretransplant immunosuppression followed by a myeloablative reduced-toxicity conditioning regimen (fludarabine and i.v. busulfan [Flu-IV Bu]) and then HSCT. The median patient age was 15 years (range, 10 to 20 years). Before the Flu-IV Bu + antithymocyte globulin conditioning regimen, all patients received 1 to 2 cycles of pretransplant immunosuppression with fludarabine and dexamethasone. Fifteen patients received a related donor graft, and 6 received an unrelated donor graft. An initial prompt engraftment of donor cells with full donor chimerism was observed in all 18 patients, but 2 patients developed secondary mixed chimerism that necessitated withdrawal of immunosuppression to achieve full donor chimerism. Three patients (14%) had acute grade III-IV graft-versus-host disease, and 5 patients had limited chronic graft-versus-host disease. The only treatment-related mortality was from infection, and with a median follow-up of 50 months (range, 4 to 83), the 5-year overall survival and thalassemia-free survival were 93%. We conclude that this novel sequential immunoablative pretransplantation conditioning program is safe and effective for patients with high-risk class 3 thalassemia exhibiting additional comorbidities.

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Outcome Of Hematopoietic Stem Cell Transplantation For Wiskott-Aldrich Syndrome

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Wiskott-Aldrich syndrome (WAS) is an X-linked immunodeficiency presented with eczema, microthrombocytopenia, autoimmune disorders, recurrent infections, and subsequent malignancies. Little is known on late complications following hematopoietic stem cell transplant (HSCT) in this population. In a single-institutional retrospective study of 17 WAS patients who underwent HSCT between January 1992 and December 2012, we evaluated autoimmune manifestations, serious infections, and graft-versus-host disease (GVHD).

Median age at HSCT was 2.17 years (range 0.28-12.38). Nine (52.9%) and eight patients (47.1%) received bone marrow and umbilical cord blood, respectively. Fourteen patients (82.3%) underwent HSCT from alternative donors including unrelated cord, mismatch family, and match unrelated donors. Only 2 match sibling (11.7%) and one match related (5.9%) were used as donors. Median follow-up time was 7.05 years (range 1.82-19.99).

Two patients (11.7%) died 1 month and 2.1 years post HSCT due to CMV interstitial pneumonitis and severe *Streptococcus pneumoniae* sepsis, respectively. Overall survival (OS) at 2-year was 87.4%. HLA mismatch and stem cell source were not significant factors for OS (p= 0.325 and 0.886, consecutively). In multivariate analysis, age at HSCT, HLA mismatch, and stem cell sources were also not significant.

Five patients (29.4%) developed acute GVHD grade II-IV. The incidence of acute GVHD (grade II-IV) was higher when using bone marrow as a stem cell source (p= 0.029). Eight (47.1%) and three patients (17.6%) developed limited and extensive GVHD. The incidence of chronic GVHD did not differ by age at HSCT, HLA mismatch, and stem cell source.

Mixed donor chimerism was temporarily observed in 4 patients (23.5%). Immunosuppressant was adjusted without donor lymphocyte infusion. Donor chimerism was subsequently improved.

We observed chronic GVHD-independent autoimmune thrombocytopenia in 4 patients (23.5%). One of those four also developed warm and cold agglutinin positive autoimmune hemolytic anemia. All episodes of autoimmune thrombocytopenia occurred in patients who received cord blood transplantation. Mixed donor chimerism was observed in 3 of those 4 patients who had persistent thrombocytopenia. Only one patient who developed autoimmune thrombocytopenia and hemolytic anemia received treatment of plasmapheresis and rituximab. This patient eventually required regular intravenous immunoglobulin infusion due to persistent hypogammaglobulinemia. Thrombocytopenia was gradually subsided with the improvement of donor chimerism in all patients. No malignancy occurred post-HSCT in this retrospective cohort.

We report an excellent result using a majority of unmanipulated unrelated and mismatched family donors in this study. Cytopenias were observed in conjunction with utilization of cord blood stem cells and mixed donor chimerism.

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A Novel Reduced Intensity Conditioning Regimen for Patients with High Risk Hematologic Malignancies Undergoing Conventional Allogeneic Stem Cell Transplantation

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Introduction: Reduced intensity conditioning (RIC) allows older patients and those with comorbidities to undergo